was of advanced reproductive age were lighter than those in which the breeders were age-matched (e.g., pups from YFOM breeders were lighter than those from YFYM breeders).

CONCLUSIONS: Parental age impacted fertility outcomes, with the YFOM group having the highest fecundity and OFOM the lowest. Maternal age dictated litter size, with breeding pairs with old females (OFYM and OFOM) having the smallest litters. Emerging relationships between parental age and body weight in male and female offspring may have significant health impacts long term.

IMPACT STATEMENT: Advanced age results in cumulative exposures that influence reproductive function in the parental generation and may have a multi-generational impact. Studies are ongoing to evaluate the reproductive and general health outcomes in the male and female offspring derived from the parental breeding groups.

P-771 6:30 AM Wednesday, October 20, 2021

INDOMETHACIN CAN PROTECT PLACENTAL INFLAMMATION AND DELAY PRETERM BIRTH IN THE LPS-INDUCED PRETERM DELIVERY MODEL. Sema Avci, Ph.D, Asst. Prof.,[1] Nilay Kuscu, PhD,[2] Begum Durkut, M.Sc. Student,[2] Leyla Kilinc, M.Sc,[2] Ismail Ustunel, Ph.D, Prof.,[2] Ciler Celik-Ozenci, DDS, PhD Prof[2] [1]Alaaddin Keykubat University, Antalya, Turkey; [2]Akdeniz University, Antalya, Turkey.

OBJECTIVE: The major cause of prematurity is preterm birth (PTB), associated with intrauterine inflammation. Defects in the Notch pathway harm placentation, and there is evidence between Notch activation and the inflammatory environment. In the action of PTB, surfactant A (SP-A) may have a pro-inflammatory or anti-inflammatory effect, and increased synthesis of prostaglandins illustrates their crucial roles in gestational tissues at parturition. Altogether, the potential of SP-A and prostaglandin inhibitors to prevent PTB through the placenta is worth exploring. This study evaluates the preventive effect of SP-A and Indomethacin (IND) treatment on placental inflammation in the LPS-induced PTB model.

MATERIALS AND METHODS: Forty-eight female CD-1 mice were distributed to pregnant control (PC), Sham, PBS, IND (2 mg/kg; intraperitoneally), LPS (25μg/100μl; intrauterine), LPS+IND, SP-A block (SP-A B; 20ug/100μl; intrauterine) groups. The injections were performed on day 14.5 of pregnancy. Placentae were removed on day 15.5 of pregnancy, and immunohistochemical analyzes were performed. Differences in staining intensities between the groups for Cox-1, Notch-1 (N1), Dll-1, Jagged-2 (Jag-2), SP-A, Tlr-2, and Tlr-4 proteins were compared using ANOVA and Sidak's Multiple Comparison test. P values <0.05 were considered statistically significant.

RESULTS: PTB rates were; 100%, 66% (in this group, delivery delayed for about 5 hours), and 50% in LPS, LPS+IND, SP-A B groups, respectively. LPS application caused damage to fetal and maternal vascular structures in the placenta, especially in the labyrinth zone (LZ). Placental volume decreased, and lymphocyte infiltration was observed. The morphological distinction between the compartments was unclear. N1 expression increased in both the junctional zone (JZ) and LZ. Cox-1 expression in the LZ decreased significantly ($p<0.05$), while the expression of N1, Dll- 1, and Jag-2 increased significantly ($p<0.05$). Tlr-2 and Tlr-4 expression increased significantly in LZ and JZ, respectively. In the LPS+IND group, the LZ morphology was similar to the control, and placenta zone boundaries were distinguishable. In the LPS+IND group, N1, Jag-2, and Tlr-4 expression decreased significantly ($p<0.05$). In the SP-A B group, Cox-1 expression increased significantly ($p<0.05$).

CONCLUSIONS: In the PTB model, Notch signaling, SP-A, and prostaglandin-associated signaling are disturbed in the maternal-fetal exchange site, the LZ and hormonal production site, the JZ of the placentae. While SP-A modulates the LPS-induced inflammatory response related to PTB, IND can prevent PTB via decreasing inflammation in the LZ.

IMPACT STATEMENT: Activation of inflammatory signaling pathways can cause damage to the placenta during inflammation-related PTB. Our results highlight the necessity of future clinical studies utilizing prostaglandin inhibitors to improve the placental function in preventing this process.

SUPPORT: International Joint Doctorate Fellowship Program of TUBITAK (2214/A to Avci S.,G.N:1059B141700505) and Akdeniz University Research Foundation (TD**K-201**8-3256).

P-772 6:30 AM Wednesday, October 20, 2021

FORMONONETIN INHIBITS PROLIFERATION OF ENDOMETRIOSIS VIA DOWN-REGULATION OF P27-PERK-PSTAT3-TWIST1 PATHWAY. Yunjeong Park, M.D.,[1] Jae Hoon Lee, M.D.,[2] Sihyun Cho, M.D., Ph.D.,[1] Sung Pil Choo, M.D.,[1] Heeyon Kim, M.D.,[3] Inha Lee, M.D.,[4] Young Sik Choi, M.D., Ph.D.,[5] Byung Seok Lee, M.D., Ph.D.[2] [1]Yonsei University College of Medicine, Gangnam Severance Hospital, Seoul, Korea, Republic of (South); [2]Severance Hospital, Seoul, Korea, Republic of (South); [3]Yonsei University College of Medicine, Severance hospital, Seoul, Korea, Republic of (South); [4]Yonsei University College of Medicine, Seoul, Korea, Republic of (South); [5]Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of (South).

OBJECTIVE: Formononetin is a phytoestrogen known to function as a selective estrogen receptor modulator. We aimed to evaluate the effect of formononetin on proliferation of endometriosis in this study

MATERIALS AND METHODS: We obtained eutopic endometrium from patients diagnosed endometriosis after surgery. To determine therapeutic dose of formononetin, the concentration in 70% of cells that survived when formononetin was administered was calculated through the CCK8 assay. While increasing the formononetin concentration up to the corresponding concentration, the target protein expression level of the endometriotic endometrium was measured by western blot. Statistical analysis was calculated using SPSS 25, IBM. Significant differences were assessed using Mann-Whitney tests. A p-value <0.05 was considered statistically significant

RESULTS: We set the maximum concentration of formononetin administration to 80μM through the CCK8 assay. The expression levels of pAKT, pERK, p27, p53, and BAX proteins were evaluated by western blot by increasing formononetin in steps of 20μM. (N=4) In this experiment, the expression of pERK, twist1 decreased after 20μM, and p27, pSTAT3 decreased depending on the concentration increase. ($p<0.05$) On the other hand, pAKT, p53, and BAX did not show any significant difference.

CONCLUSIONS: Formononetin could inhibit proliferation of endometriosis with dose dependent manner in vitro, with downregulation of p27, pERK, pSTAT3, and Twist1.

IMPACT STATEMENT: Results of this study suggest that formononetin may be used as a therapeutic agent for endometriosis. In vivo and clinical studies are warranted to confirm findings of this study.

P-773 6:30 AM Wednesday, October 20, 2021

SODIUM TUNGSTATE INCREASES EMBRYO IMPLANTATION AND REPRODUCTIVE EFFICIENCY IN SPRAGUE-DAWLEY RATS. Ignasi Canals, Ph.D.,[1] Rosa Torres, Ph.D.,[1] Eduardo Cunchillos, Ph.D.,[2] Arbat Agnes, MD.[1] [1]Oxolife SL, Barcelona, Spain; [2]Innoqua Toxicology Consultants S.L, Barcelona, Spain.

OBJECTIVE: To evaluate sodium tungstate (ST) effects on reproductive outcomes in Sprague Dawley rats

MATERIALS AND METHODS: 8-9 week-old Crl:CD female rats were randomized into four groups. ST (40 (D1), 80 (D2), or 160 (D3) mg/kg/day) or vehicle were administered during at least 20 days, covering the premating period (14 days) until implantation of the conceptus (day 6 of gestation). After mating with competent males (ratio 1:1), mated females, confirmed by sperm presence in vaginal smears, were housed individually. Mated females were sacrificed on the 13th gestation day. Corpora lutea (CL) and implanted embryos (IE) were recorded. Implantations were classified as early intrauterine deaths, dead embryos, or viable embryos (VE). For groups comparison of fertility values ANOVA and Student's test were used. For comparison of percentages of success, a linear model with a binomial distribution using the "glm" function from the "stats" R [1] package was used.

RESULTS: All mated females became pregnant in this study independently on the treatment dose or placebo. Evaluated fertility parameters are described in the table.

Results show that despite the high fertility performance of the placebo group, ST enhances embryo implantation and the viability of implanted embryos with a statistical significance at D2 (11.8% and 9.3% increase of VE and IE respectively), and with a clear trend at D1 (5.2% and 4.3% increase

	Placebo (n=19)	ST dose (mg/Kg/day)		
		40 (n=18)	80 (n=16)	160 (n=19)
Num. of CL	16.7±1.5	17.3±1.5	17.8±1.3*	16.6±1.4
Num. of IE	16.1±1.7	16.8±1.0[#]	17.6±1.5**	16.2±1.5
Num. of VE	15.3±1.9	16.1±1.1[#]	17.1±1.7**	15.7±1.6
% of implanted embryos (IE/CL)	96.5±4.6	97.7±4.1	98.9±3.3[#]	97.7±3.8
% of Implantation (VE/IE)	95.1±4.9	95.8±4.4	97.0±4.2	97.2±5.1
% of viable implanted embryos (VE/CL)	91.7±6.5	93.6±7.0	96.0±5.9*	94.9±5.5

*mean±SD. *p<0.05; **p<0.01; [#]p=0.06*

of VE and IE respectively) when compared with placebo. No differences were observed between placebo and D3. Moreover, an increase in ovulation is observed only with D3. Implantation parameters normalized to CL show an increase in the percentage of viable implanted embryos (p>0.05) and percentage of implanted embryos (p=0.06). Additional analysis reveals that all embryos and females were healthy with no reprotoxic effects observed in any of the studied doses.

CONCLUSIONS: Oral sodium tungstate treatment improves fertility in Sprague Dawley rats due to the direct effect of increasing embryo implantation. Additionally, it also enhances ovulation.

IMPACT STATEMENT: Our results support sodium tungstate as a potential treatment for infertility acting on embryo implantation, a currently unmet medical need.

P-774 6:30 AM Wednesday, October 20, 2021

PRO- AND ANTI-INFLAMMATORY CYTOKINES (TNF-A, IL-6, IL-4, IL-10) SECRETION FROM PBMC. Rumiana Ganeva, MSc, Dimitar Parvanov, PhD, Maria Handzhiyska, MSc, Georgi Stamenov, MD/PhD Nadezhda Women's Health Hospital, Sofia, Bulgaria.

OBJECTIVE: To observe the pro- and anti-inflammatory cytokine (TNF-α, IL-4, IL-6, IL-10) secretion from cultivated peripheral blood mononuclear cells (PBMCs) for 48h.

MATERIALS AND METHODS: Blood samples were obtained from 42 women patients of Nadezhda Women's Health Hospital after signing written informed consent. For PBMC isolation, 9 ml of heparinised whole blood from each patient were processed by density gradient centrifugation using Pancoll (P04-60100, Pan-Biotech) for 25 minutes at 400G. The buffy coat of PBMCs were collected and washed with phosphate buffer saline. A total of $5x10^6$ /ml cells were cultured in 0.5 ml RPMI medium (R-8758, Sigma) supplemented with 1% HSA (GHSA-125, LifeGlobal) for 48 hours at 37oC. Concentrations of tumor necrosis factor alpha (TNF-α), interleukin-6 (IL-6), interleukin-4 (IL-4) and interleukin-10 (IL-10) in the PBMC media were measured by sandwich enzyme-linked immunosorbent assay (ELISA) (CSB-E04638h, CSB-E04740h, CSB-E04633h and CSB E04593h, Cusabio Technology, respectively) according to the manufacturers' instructions.

Results are presented as mean ±SD and range. Descriptive statistics and one-way ANOVA with post hoc LSD were performed with SPSS Software ver. 21. P<0.05 was considered significant.

RESULTS: No cytokines were detected in the clear RPMI media control. The presence of IL-4, IL-6, IL-10 and TNF-α was confirmed in all PBMC samples.

The proinflammatory cytokines (IL-6 and TNF-α) concentrations in the PBMC culture media after 48h of cultivation were 90.48±89.1 pg/ml (range: 25.05 – 266.43) and 510.36±66.81 pg/ml (range: 400.59 – 565.10), respectively.

The mean concentrations of the anti-inflammatory cytokines (IL-4 and IL-10) secreted from the PBMC at the 48h of cultivation were 438.82±130.27 pg/ml (range: 227.53 - 599.19) and 4667.33±3505.7 pg/ml (range: 1808.31 – 9964.99), respectively.

Additionally the secretion of IL-10 was significantly higher in comparison to the other analysed cytokines (p<0.001).

CONCLUSIONS: Results from this study showed that PBMCs secrete detectable amounts of pro- and anti-inflammatory cytokines in the culture media. Furthermore the PBMC culture supernatant had significantly higher amount of IL-10 in comparison to the other studied cytokines (IL-4, IL-6 and TNF- α).

IMPACT STATEMENT: The intrauterine administration of autologous PBMC was proposed as an effective approach to improve embryo implantation in patients with repeated IVF failures. Knowledge of the basic cytokine secretion from PBMC could navigate the future research on the modulation of PBMC cytokine secretion to favour the embryo implantation.

SUPPORT: N/A

POSTER SESSION: REPRODUCTIVE SURGERY

P-775 6:30 AM Wednesday, October 20, 2021

FOLLICULAR ACTIVATION IN POOR OVARIAN RESPONDERS (FAPPOR): A RANDOMIZED CONTROLLED TRIAL. Cesar Diaz-Garcia, M.D., M.P.H., Ph.D.,[1] Sonia Herraiz, Ph.D.,[2] Loida Pamplona, M.D., Ph.D.,[3] Jessica Subirá, M.D., Ph.D. student,[3] María José Soriano, MSc, Ph.D. student,[2] Carlos Simón, MD, PhD,[4] Emre Seli, M.D.,[5] Antonio Pellicer, M.D., Ph.D.[6] [1]Medical Director IVI LONDON, London, United Kingdom; [2]IVI Foundation Innovation - Reproductive Medicine IIS La Fe, Valencia, Spain; [3]La Fe University Hospital, Valencia, Spain; [4]Professor University of Valencia, INCLIVA, Founder and Head of the Scientific Advisory Board, Igenomix, Paterna (Valencia), Spain; [5]IVI RMA New Jersey, Basking Ridge, NJ; [6]IVIRMA Rome, Rome, Italy.

OBJECTIVE: Mechanical fragmentation of the ovarian cortex to activate dormant follicles by suppressing the Hippo pathway (called in vitro activation [IVA] or ovarian fragmentation for follicular activation [OFFA]) has been proposed as a therapeutic option for women with poor ovarian response (POR) and premature ovarian insufficiency (POI). A number of case series and cohort studies suggested improved reproductive outcomes with ovarian fragmentation, either alone (drug-free) or in combination with biomolecules that act upon the Akt/PTEN pathway to further promote follicular activation. In this study we aimed to investigate if ovarian fragmentation improves ovarian reserve markers and IVF outcomes in women with POR.

MATERIALS AND METHODS: Randomized controlled trial (NCT02354963). Thirty-four women with POR according to ESHRE Bologna criteria who were < 40 years of age were randomized to undergo ovarian fragmentation by laparoscopy in one ovary (n=16), or to no intervention (control group, n=18). Ovarian reserve markers were followed biweekly for 6 months and IVF cycles initiated when patients doubled antral follicle count (AFC) or at the end of follow-up.

RESULTS: Baseline characteristics for enrolled patients showed no difference between the groups. Ovarian fragmentation was performed in 15 women and effectiveness of the procedure was confirmed by detecting an 18.8% reduction in the phospho-YAP/YAP protein ratio and increased *BIRC* and *CCN* gene expression after fragmentation (p<0.05 for each). Ovarian fragmentation resulted in an increase in the AFC in the intervention ovary compared to the control ovary in the same patient (p=0.048). When control and surgery groups were compared, total AFC was increased in the intervention group (p=0.021) due to the improvement in the number of follicles in the ovary in which ovarian fragmentation was carried out (p=0.008). However, serum AMH or FSH levels were not different before or after the surgery or between the groups. Following the intervention, 15 patients from each arm underwent at least 1 IVF cycle. In the control group, 33 MII oocytes were retrieved, 28 cleavage stage embryos developed and 18 embryo transfers (ETs) were performed with 20% pregnancy rate (PR) and 18.7% live birth rate (LBR) per cycle. In the surgery group, 23 MII oocytes were retrieved, 12 embryos developed, and 11 ETs were performed with 13.3% PR and 6.7% LBR per cycle. Statistically significant differences were not detected in any of the IVF-related outcomes between study groups. A total of 3 pregnancies and 4 live births (1 twin pregnancy) were recorded in the control group, while 2 pregnancies and 1 healthy live birth were recorded in the surgery group.